363P- A multicenter, real-world observational study of efficacy and safety of first-line osimertinib treatment in patients with epidermal growth factor receptor (EGFR) activating mutation-positive advanced non-small cell lung cancer (Reiwa study)

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Comprehensive Support Project

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Background

- Osimertinib is a third-generation, irreversible EGFR-TKI that selectively inhibits both EGFR-TKI-sensitizing and EGFR-T790M (resistant) mutations.
- In a phase III trial (FLAURA), osimertinib showed efficacy superior to that of first-generation gefitinib and erlotinib, with a similar safety profile and lower rates of serious adverse events.
- Osimertinib is currently being used as the first-line treatment for patients with advanced EGFR mutation-positive NSCLC.
- However, the efficacy and safety of osimertinib treatment in real-world clinical practice have not been fully verified.

Methods

【Design】
- A multicenter, prospective cohort study in Japan

【Patients】
- EGFR mutation-positive
- Advanced or recurrent NSCLC patients
- Started EGFR-TKI treatment from September 2018 to August 2020 were enrolled
- Those receiving first-line osimertinib monotherapy were followed-up for clinical courses.

【Primary endpoint】
- Progression free survival (PFS) with osimertinib

EGFR mutation-positive NSCLC From Sep 2018 to Aug 2020

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Obtained consent (n=660) → Ineligible (n=1)

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Osimertinib (n=583)

↓

A survey was conducted once every six months

Other EGFR-TKI (n=76)

Follow-up period median 24.6 months (range, 0.1-42.0)

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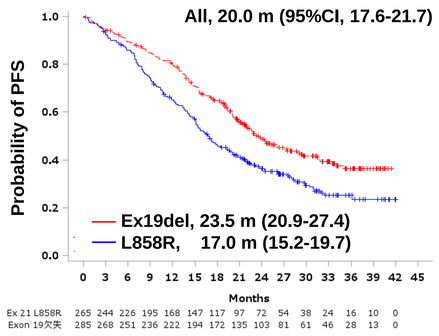
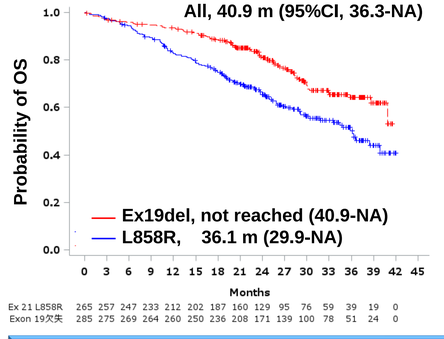
Patient Characteristics (n=583)

	n (%)
Age, years	
median (range)	72 (30-95)
Gender	
male	224 (38.4)
female	359 (61.6)
ECOG PS	
0	216 (37.1)
1	281 (48.2)
2	60 (10.3)
3	20 (3.4)
4	2 (0.3)
missing	4 (0.7)
Smoking status	
never	325 (55.8)
former	224 (38.4)
current	34 (5.8)
Histology	
adeno	571 (97.9)
squamous	9 (1.5)
NOS	2 (0.3)
LCNEC	1 (0.1)
Mutation type*	
Ex19del	285 (48.9)
L858R	266 (45.6)
others	33 (5.7)
Stage	
locally advanced	9 (1.5)
metastatic	384 (65.9)
recurrence	190 (32.6)
Brain metastases	
yes	169 (29.0)
no	414 (71.0)

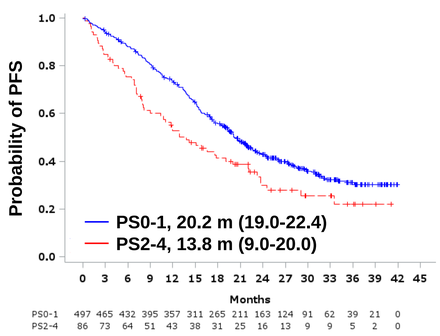
*One patient had both Ex19del and L858R mutations

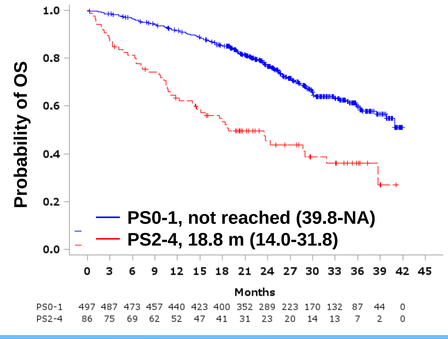
Survival by mutation type





Survival by ECOG PS

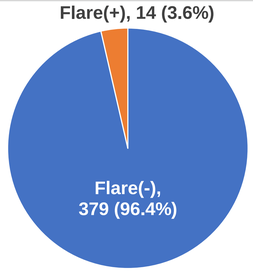




Adverse events

Pneumonitis, n (%)	PS 0-1	PS 2-4
Any grade	**67 (13.4)**	**8 (9.3)**
Grade 1	19 (3.8)	2 (2.3)
Grade 2	34 (6.8)	2 (2.3)
Grade 3	10 (2.0)	2 (2.3)
Grade 4	4 (0.8)	2 (2.3)
Grade 5	0	0

Disease flare



Flare defined as rapid disease deterioration within one month resulting in hospitalization or death, after discontinuation of osimertinib treatment, except in case of causes not directly related to NSCLC exacerbation

AE ≧ Grade 3, n (%)	PS 0-1	PS 2-4
All events	**105 (21.3)**	**27 (31.4)**
Pneumonitis	14 (2.8)	4 (4.7)
Rash	14 (2.8)	3 (3.5)
AST/ALT increased	10 (2.0)	3 (3.5)
Neutropenia	9 (1.8)	1 (1.2)
Paronychia	9 (1.8)	0 (0)
Anorexia	8 (1.6)	3 (3.5)
Anemia	7 (1.4)	3 (3.5)
Diarrhea	4 (0.8)	2 (2.3)
Thrombocytopenia	4 (0.8)	1 (1.2)
Leukopenia	3 (0.6)	1 (1.2)
Prolonged QT interval	2 (0.4)	2 (2.3)

AE leading to discontinuation, n (%)	PS 0-1	PS 2-4
All events	**95 (19.1)**	**21 (24.4)**
Pneumonitis	48 (9.7)	5 (5.8)
Hematotoxicity	6 (1.2)	1 (1.2)
Rash	6 (1.2)	5 (5.8)
Paronychia	6 (1.2)	0 (0)
AST/ALT increased	3 (0.6)	2 (2.3)
Prolonged QT interval	1 (0.2)	2 (2.3)

Exacerbation pattern

n (%)	Asymptomatic and no clinical exacerbation	Symptomatic and no clinical exacerbation	Clinical exacerbation	total
CNS metastasis	15 (4.8)	4 (1.3)	17 (5.4)	36 (11.4)
Single organ other than CNS (up to 3 per organ)	94 (30.0)	28 (8.9)	16 (5.1)	138 (43.7)
Multiple organs	66 (20.9)	37 (11.7)	39 (12.3)	142 (44.9)
Total	175 (55.4)	69 (21.8)	72 (22.8)	316 (100)

Conclusion

- Osimertinib showed activity with a manageable safety profile in clinical practice, consist with results of previous clinical trials.
- Efficacy was different according to mutation type.
- More evidence is needed for patients with poor PS.

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